

LISTING OF THE CLAIMS

The listing of claims will replace all prior versions, and listings of the claims in the application:

1. (Presently Amended) An abuse-resistant controlled-release pharmaceutical composition~~[[,]]~~ comprising a plurality of microspheres, each ~~microspheres comprising comprises;~~

(i) a water insoluble matrix material, and containing

(ii) a plurality of discrete particles distributed throughout the water insoluble matrix material, each particle comprises ~~[[of]]~~ a pharmaceutically effective amount of an active water soluble compound capable of abuse wherein said discrete particles (1) comprise micronized particles of said water soluble compound and having surfaces that are wetted with a coating of said the water insoluble matrix material, and (2) are distributed throughout said microsphere within a matrix of said water insoluble matrix material;

wherein said water insoluble matrix material is a viscoelastic polymer elastic and present in an abuse-reducing amount whereby ~~such that~~ crushing, compressing, fracturing, tumbling, rolling, or milling of said controlled-release pharmaceutical composition results in an including said microspheres before coming in contact with an aqueous environment increase~~[[s]]~~ in the aqueous dissolution of said active water soluble compound ~~in said microspheres~~ by less than about 15% of the total said pharmaceutically effective amount of the active water soluble compound in the composition in the first hour of in vitro dissolution testing.

wherein the water soluble compound capable of abuse is an opioid agonist,
and

wherein the composition does not include an antagonist of the water soluble compound capable of abuse ~~does not substantially modify the dissolution rate of said active water soluble compound thereafter.~~

2 to 3. Cancelled.

4. (Presently Amended) The ~~[[An]]~~ abuse-resistant composition according to claim 1 wherein said matrix material is non-erodable at pH less than about 6.

5. (Presently Amended) The ~~[[An]]~~ abuse-resistant composition according to claim 4 wherein said matrix material is erodable in the presence of bile salts and lipase.

6. Cancelled.

7. (Presently Amended) The ~~[[An]]~~ abuse-resistant composition according to claim 1 wherein said compound is a narcotic.

8. Cancelled.

9. (Presently Amended) The ~~[[An]]~~ abuse-resistant composition according to claim 1 wherein crushing said matrix before contacting with water increases the aqueous dissolution of active water soluble compound in said composition by less than about 10% of the total said pharmaceutically effective amount of the active water soluble compound in the composition in the first hour of in vitro dissolution testing, and wherein the composition does not include an antagonist of the water soluble compound capable of abuse ~~does not substantially modify the dissolution rate of said active water soluble compound thereafter.~~

10. Cancelled.

11. (Presently Amended) The ~~[[An]]~~ abuse-resistant controlled-release pharmaceutical composition according to claim 1 for administration to a subject in need thereof from once to four times a day.

12. (Withdrawn) A method for the preparation of an sustained release pharmaceutical composition having a reduced potential for abuse, comprising:

providing a pharmaceutically active compound capable of inducing in a subject a reaction that is physiologically or psychologically addictive if administered in an immediate release dosage form;

applying a pressure force to a mixture comprising particles of said compound and a water insoluble material thereby resulting in surface coated particles; and

incorporating said surface coated particles into a pharmaceutical composition that when subjected to stress does not increase substantially the immediate release of said compound in an aqueous environment.

13. (Withdrawn) A method according to claim 12 wherein said force is applied to a dispersion of said particles in a flowable medium comprising said material.

14. (Withdrawn) A method according to claim 13 wherein said force is an abrupt pressure force.

15. (Withdrawn) A method according to claim 13 wherein said force is an ultrasonic force.

16. (Withdrawn) A method according to claim 13 wherein said force is piston generated shock wave.

17. (Withdrawn) A method according to claim 13 wherein said particles are micronized.

18. (Withdrawn) A method according to claim 17 wherein said particles have a mean particle wave size of less than about ten microns.

19. (Withdrawn) A method according to claim 13 wherein said material comprises a polymorphic wax.

20. (Withdrawn) A method according to claim 19 wherein said wax comprises a hydrogenated vegetable wax, a tri-, di- or mono-glyceride, or a mixture thereof.

21. (Withdrawn) A method according to claim 20 wherein said material comprises a polymeric material that is water insoluble, and erodable in the intestinal tract at pH greater than about 6.

22. (Withdrawn) A method according to claim 13 further comprising solidifying said dispersion into microspheres.

23. (Withdrawn) A method according to claim 12 wherein the application of mechanical stress to said composition modifies the aqueous dissolution of said compound by an increase of less than about 15% of said pharmaceutically effective amount in the first hour, and does not substantially modify the dissolution rate of said composition thereafter.

24. (Presently Amended) The dosage form according to claim 7 wherein said narcotic is selected from the group consisting of fentanyl, sufentanil, carfentanil, lofentanil, alfentanil, hydromorphone, oxycodone, hydroxycodone, propoxyphene, ~~pentazocine~~, methadone, tilidine, butorphanol, buprenorphine, levorphanol, codeine, oxymorphone, meperidine, dihydrocodeinone and cocaine.

25. Cancelled.

26. Cancelled.

27. (New) An abuse resistant pharmaceutical composition consisting essentially of:

a hard gelatin capsule encapsulating:

(i) a plurality of immediate release microspheres of a hydrophobic polymer matrix having dispersed therein, an active ingredient capable of abuse in an amount sufficient to provide a T_{max} of from 2 to 4 hours; and

(ii) a plurality of controlled release microspheres of a water insoluble matrix of organic material resistant to dissolution or acidic degradation at pH less than 4, having a size in the range from 50 to 800 microns, having dispersed therein, an active ingredient capable of abuse, which is the same or different from the active ingredient in the immediate release microspheres, and having a surface coating material comprising methylmethacrylate or ethylcellulose on the surface of the microspheres,

wherein the pharmaceutical composition releases the active ingredient at a rate that blood plasma concentrations are maintained within a therapeutic range over a period of time from 8 to 24 hours, and further wherein the composition does not include an antagonist of the water soluble compound capable of abuse.

28. (New) The abuse-resistant composition according to claim 27, wherein said matrix material is non-erodable at pH less than about 6.

29. (New) The abuse-resistant composition according to claim 27 wherein said matrix material is erodable in the presence of bile salts and lipase.

30. (New) The abuse-resistant composition of claim 27, wherein the water insoluble matrix of organic material is selected from the group consisting of ethylcellulose, cellulose acetate, vinyl acetate/vinyl chloride copolymers, acrylate/methacrylate copolymers, polyethylene oxide, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, triglycerides, hydrogenated vegetable oils, triglyceride polyalkoxyalkylesters, fats, waxes, water insoluble partially-degraded proteins and mixtures thereof.

31. (New) The abuse-resistant composition according to claim 27 wherein said compound is an analgesic opiate narcotic.

32. (New) The abuse-resistant composition to according to claim 31 wherein said narcotic is selected from the group consisting of hydromorphone, oxycodone, hydroxycodone, propoxyphene, methadone, tilidine, butorphanol, buprenorphine, levorphanol, codeine, oxymorphone, meperidine, dihydrocodeinone.

33. (New) An abuse resistant pharmaceutical composition consisting essentially of:

(a) a polymeric matrix composition consisting essentially of a polymeric moiety and from about 1 to about 50% of an aliphatic alcohol having from 8 to 20 carbon atoms, based on the weight the total matrix composition,

(b) particles of an active ingredient capable of abuse having a water insoluble controlled release surface coating thereon, the particles being chemically bonded to the polymeric matrix, whereby the active ingredient capable of abuse is substantially incapable of immediate release from the polymeric matrix, and further wherein the composition does not include an antagonist of the water soluble compound capable of abuse.

34. (New) The abuse-resistant composition according to claim 33, wherein said aliphatic alcohol is fatty alcohol.

35. (New) The abuse-resistant composition according to claim 34, wherein said fatty alcohol is selected from the group consisting of cetyl alcohol, stearyl alcohol and a combination thereof.
36. (New) The abuse-resistant composition according to claim 33 wherein said matrix material is erodable in the presence of bile salts and lipase.
37. (New) The abuse-resistant composition according to claim 33 wherein said compound is an analgesic opiate narcotic.
38. (New) The abuse-resistant composition according to claim 33 wherein said narcotic is selected from the group consisting of hydromorphone, oxycodone, hydroxycodone, propoxyphene, methadone, tilidine, butorphanol, buprenorphine, levorphanol, codeine, oxymorphone, meperidine, dihydrocodeinone.
39. (New) The abuse-resistant composition of claim 33, wherein the polymeric moiety is a polymer selected from the group consisting of ethylcellulose, cellulose acetate, vinyl acetate/vinyl chloride copolymers, acrylate/methacrylate copolymers, polyethylene oxide, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, triglycerides, hydrogenated vegetable oils, triglyceride polyalkoxyalkylesters, fats, a hydrogenated cottonseed oil wax, a partially hydrogenated soybean oil, carnuba wax, water insoluble partially-degraded proteins and mixtures thereof.
40. (New) The abuse-resistant composition of claim 1, wherein the viscoelastic polymer is a triglyceride wax selected from the group consisting of a hydrogenated cottonseed oil wax, a partially hydrogenated soybean oil, carnuba wax or a mixture thereof.